Int J Clin Exp Med 2019;12(8):10668-10674
www.ijcem.com /ISSN:1940-5901/IJCEM0094930

Original Article

Efficacy of fluoxetine combined with psychological intervention for treatment of depressive patients with insomnia

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Received April 5, 2019; Accepted June 10, 2019; Epub August 15, 2019; Published August 30, 2019

Abstract: Objective: The aim of the current study was to investigate the clinical effects of fluoxetine combined with psychological intervention on depressive patients with insomnia, examining influences on sleep quality and quality of life. Methods: One hundred and seventy-eight patients with depression and insomnia were selected as research subjects. A total of 98 patients were treated with fluoxetine combined with psychological intervention (group A). A total of 80 patients were treated with fluoxetine only (group B). Clinical therapeutic effects of the two groups were observed. Depression degrees of the patients were evaluated via Hamilton depression rating scale (HAMD) scores. Sleep quality was assessed using Pittsburgh Sleep Quality Index (PSQI) scores. Quality of life, after treatment, was evaluated by World Health Organization Quality of Life-Brief (WHOQOL-BREF) scores. Incidence of adverse reactions in the two groups was observed. Results: There were no significant differences in HAMD scores and PSQI scores between groups A and B before treatment (both $P>0.05$). Scores in both groups decreased significantly after treatment (both $P<0.001$). After treatment, HAMD scores and PSQI scores in group A were significantly lower than those in group B (both $P<0.001$). Reduction rates in group A were significantly higher than those in group B (both $P<0.001$). There were no significant differences in incidence of adverse reactions between groups A and B ($P>0.05$). After treatment, scores of mental health, physiological health, surrounding environment, and social relations via the WHOQOL-BREF scale in group A were significantly higher than those in group B (all $P<0.001$). Conclusion: Fluoxetine combined with psychological intervention demonstrated good clinical effects on depressive patients with insomnia, significantly reducing depression, improving sleep quality, and improving quality of life. Therefore, it is worthy of clinical application and promotion.

Keywords: Depression, insomnia, fluoxetine, psychological intervention, sleep quality, quality of life

Introduction

Depression is a common affective disorder, characterized by persistent low mood and accompanied by activity decline and somatic symptoms. With the acceleration of modern society and strengthening of competition in industries, many people are under great pressure. This has resulted in an increase in incidence rates of depression [1, 2]. About 15% of people have experienced depression in their life, a frequent and common disease in society [3]. Depressive patients suffer from frequent anxiety, depression, and other adverse psychological emotions, often accompanied by sleep disorders mainly manifesting as difficulty in falling asleep, poor sleep quality, and insomnia. Frequent insomnia causes depression to worsen [4]. Depression not only affects individuals and families, but also brings economic costs to social health [5]. Therefore, methods of effective intervention have attracted the attention of scholars.

Fluoxetine has been widely used in clinic. It can significantly inhibit the reuptake of serotonin by the presynaptic membrane of neurons, increasing concentrations of serotonin in the synaptic space. Thus, it plays an anti-depression role [6]. Depressive patients with insomnia have poor

Table 1. General information (n, %) ($\bar{x}$±sd)

Category	Group A (n=98)	Group B (n=80)	t/χ^2 value	*P* value
Gender			0.867	0.352
Male	57 (58.16)	52 (65.00)		
Female	41 (41.84)	28 (35.00)		
Age (year)	35.6±4.1	35.2±4.8	0.600	0.550
Course of disease (month)	1.73±0.78	1.68±0.76	0.430	0.668
BMI (kg/m^2)	22.67±1.25	22.92±1.07		
Smoking history			0.799	0.371
Yes	40 (40.82)	38 (47.50)		
No	58 (59.18)	42 (52.50)		
Drinking history			0.432	0.511
Yes	44 (44.90)	32 (40.00)		
No	54 (55.10)	48 (60.00)		
Hypertension			0.508	0.476
Yes	9 (9.18)	10 (12.50)		
No	89 (90.82)	70 (87.50)		
Diabetes			0.564	0.453
Yes	12 (12.24)	7 (8.75)		
No	86 (87.76)	73 (91.25)		
Educational level			1.860	0.173
Primary school	4 (4.08)	8 (10.00)		
Secondary school	12 (12.24)	11 (13.75)		
Junior college	30 (30.61)	23 (28.75)		
University	52 (53.06)	38 (47.50)		
Residence			0.411	0.521
City	74 (75.51)	57 (71.25)		
Village	24 (24.49)	23 (28.75)		
Marital status			0.018	0.894
Unmarried	71 (72.45)	59 (73.75)		
Married	21 (21.43)	16 (20.00)		
Other	6 (6.12)	5 (6.25)		
Working status			0.191	0.662
Yes	51 (52.04)	39 (48.75)		
No	47 (47.96)	41 (51.25)		

Note: BMI, body mass index.

confidence and medication compliance due to long-term anxiety and depression levels, resulting in the failure of effective treatment [7]. Therefore, performance of psychological intervention while taking medicine can make patients receiving depression receive treatment respond with a positive attitude. This is of great significance for patient recovery.

At present, there are many studies concerning fluoxetine for treatment of depression. However, its combination with psychological intervention has been rarely examined [8-10]. Therefore, the current study explored the clinical effects of fluoxetine combined with psychological intervention on depressive patients with insomnia, examining influences on sleep quality and quality of life. The aim of the current study was to provide a reference basis for future treatment.

Materials and methods

General information

One hundred and seventy-eight patients with depression and insomnia, treated at the Zhenjiang Mental Health Center, from April 2012 to March 2015, were selected and divided into group A (fluoxetine combined with psychological intervention, n=98) and group B (fluoxetine only, n=80), with a random number table. There were 57 males and 41 females in group A, aged 19-41 years, with an average age of 35.6±4.1 years. The average course of disease of 1.73±0.78 months. Group B consisted of 52 males and 28 females, aged 20-49 years, with an average age of 35.2±4.8 years. The average course of disease of 1.68±0.76 months. This study was approved by the Ethics Committee of Zhenjiang Mental Health Center. All subjects and families were informed and provided consent.

Inclusion and exclusion criteria

Inclusion criteria: Conformed to the diagnostic criteria for depression in the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* [11]; Pittsburgh sleep quality index (PSQI) scores >7 [12]; Hamilton depression rating scale (HAMD, 24 items) scores ranging from 21-35 [13, 14].

Exclusion criteria: Patients with severe liver and renal dysfunction, hematological system disease, congenital heart disease, connective tissue disease, nervous system disease, endo-

Table 2. HAMD scores in the two groups before and after treatment ($\bar{x}$±sd)

HAMD score	Group A (n=98)	Group B (n=80)	t	P
Before treatment	25.74±7.76	25.37±8.31	0.306	0.760
After treatment	8.51±3.43[a]	11.63±4.61[a]	10.700	<0.001
Variation	17.43±4.21	13.83±3.76	5.952	<0.001

Note: HAMD, Hamilton depression rating scale. Compared with the same group before treatment, [a]P<0.001.

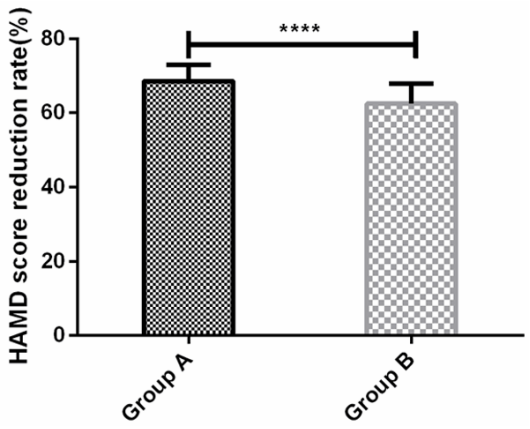

Figure 1. Comparison of HAMD score reduction rates between the two groups after treatment. HAMD, Hamilton depression rating scale. ****P<0.001.

crine and metabolic disease, and severe malnutrition; Patients combined with other mental diseases; Patients with a history of alcohol dependence or drug dependence; Patients with serious self-harm and suicide attempts; Patients with intolerance or allergic to fluoxetine.

Methods

Fluoxetine (Changzhou Siyao Pharmaceutical Co., Ltd., China, specification: 10 mg*14 tablets) was orally taken by all subjects in the morning, at a dose of 20 mg/d for 8 weeks. Patients in group A were given psychological intervention by professional psychologists once a week for 8 weeks, for a total of 90-120 minutes each time. Health education was given to the patients. Detailed causes of negative emotions were understood. Psychological counseling was performed accordingly, aiming to correct bad patient habits. Causes and harms of depression were explained and the patients were encouraged to share their experiences and opinions during treatment. Treatment methods and attention were emphasized in the process, aiming to improve the treatment compliance of patients. Each patient was encouraged to participate in aerobic exercise every day, including walking, jogging, and badminton. This was conducted to keep a relaxed mind. Moreover, the patients were guided to strengthen interpersonal communication. They were given relaxed and positive psychological support, help them to eliminate bad psychology and live positively.

Outcome measures

HAMD scale scores (5-grade scores, 0-4) was used to evaluate depression degrees of patients, including anxiety/somatization, cognitive disorders, retardation, weight loss, sleep disorders, and hopelessness. A total score >35 indicated severe depression, >20 indicated mild depression, and >8 indicated no depression. Two professionals scored patients, independently, evaluating them before and after 8 weeks of treatment.

Sleep quality of patients was evaluated with PSQI scores, including 9 self-assessment items, as well as 5 additional items. Scores ranged from 0 to 21 points. Higher scores indicate worse sleep quality. A score of 0-5 indicated very good sleep quality, 6-10 indicated good sleep quality, 11-15 indicated general sleep quality, and 16-21 indicated poor sleep quality. A total score of PSQI ≤7 was classified as normal sleep, while PSQI >7 was classified as sleep dysfunction. Two professionals scored the patients, independently, evaluating them before and after 8 weeks of treatment.

Adverse reactions in the treatment process of the two groups were observed, mainly including anorexia, sleep disorders, dry mouth, and tremors.

World Health Organization Quality of Life-Brief (WHOQOL-BREF) scores were used to assess quality of life after 6 months. Scores contained 4 dimensions, including mental health, physiological health, surrounding environment, and social relations, with a total of 26 items [15, 16]. Higher scores indicated higher quality of life.

Statistical methods

SPSS 19.0 (IBM Corp, Armonk, NY, USA) was used for statistical analysis. GraphPad Prism 7 was used to draw figures. Measurement data are expressed as mean ± standard deviation ($\bar{x}$±sd). Comparisons between groups were

Table 3. PSQI scores in the two groups before and after treatment ($\bar{x}$±sd)

PSQI score	Group A (n=98)	Group B (n=80)	t	P
Before treatment	14.21±3.24	14.16±3.19	0.103	0.918
After treatment	4.28±1.64[a]	7.05±1.81[a]	10.700	<0.001
Variation	9.97±1.67	7.05±1.32	12.730	<0.001

Note: PSQI, Pittsburgh Sleep Quality Index. Compared with the same group before treatment, [a]P<0.001.

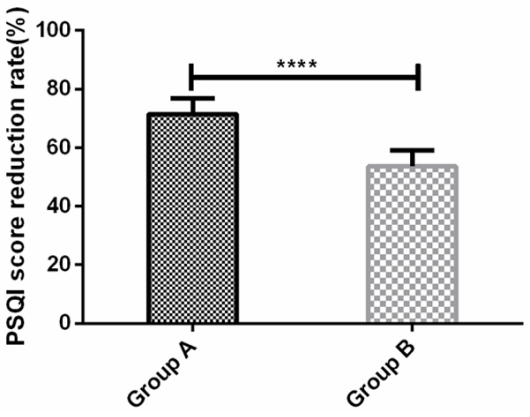

Figure 2. Comparison of PSQI score reduction rates between the two groups after treatment. PSQI, Pittsburgh Sleep Quality Index. ****P<0.001.

conducted by t-tests, while comparisons before and after treatment adopted paired t-tests. Count data are expressed by n (%). Comparisons between groups were conducted by Chi-square tests P<0.05 indicates statistical significance.

Results

General information

There were no significant differences between group A and group B in gender, age, course of disease, body mass index (BMI), smoking and drinking history, hypertension, diabetes, educational level, residence, marital status, and working status (all P>0.05). See **Table 1**.

HAMD scores in the two groups before and after treatment

The HAMD score in group A, before and after treatment, was 25.74±7.76 and 8.51±3.43, respectively. The reduction rate was (68.59±4.38)%. The HAMD score in group B, before and after treatment, was 25.37±8.31 and 11.63±4.61, respectively, with a reduction rate of (62.53±5.36)%. Therefore, there were no significant differences in HAMD scores between groups A and B before treatment (P>0.05). Scores in the two groups decreased significantly after treatment (t=27.070, P<0.001; t=17.340, P<0.001). The score in group A was significantly lower than that in group B after treatment (t=10.700, P<0.001). After treatment, the reduction rate in group A was significantly higher than that in group B (t=8.302, P<0.001). See **Table 2**, **Figure 1**.

PSQI scores in the two groups before and after treatment

The PSQI score in group A, before and after treatment, was 14.21±3.24 and 4.28±1.64, respectively. The reduction rate was (71.46±5.36)%. The PSQI score in group B, before and after treatment, was 14.16±3.19 and 7.05±1.81, respectively, with a reduction rate of (53.61±5.43)%. Thus, there were no significant differences in PSQI scores between groups A and B before treatment (P>0.05). Scores in the two groups decreased significantly after treatment (t=27.070, P<0.001; t=17.340, P<0.001). The score in group A was significantly lower than that in group B after treatment (t=10.700, P<0.001). After treatment, the reduction rate in group A was significantly higher than that in group B (t=21.970, P<0.001). See **Table 3**, **Figure 2**.

Adverse reactions in the two groups after treatment

Adverse reactions in group A and group B were mild. Most were spontaneously relieved with the extension of treatment times. In group A, anorexia occurred in 7 cases (7.14%), sleep disorders occurred in 5 cases (5.10%), dry mouth occurred in 4 cases (4.08%), and tremors occurred in 2 cases (2.04%), with an incidence of adverse reactions of 18.37%. In group B, anorexia occurred in 6 cases (7.50%), sleep disorders occurred in 6 cases (7.50%), dry mouth occurred in 5 cases (6.25%), and tremors occurred in 1 case (1.25%), with an incidence of adverse reactions of 22.50%. Therefore, there were no significant differences in incidence of adverse reactions between the two groups (all P>0.05). See **Table 4**.

Table 4. Adverse reactions in the two groups after treatment (n, %)

Group	Group A (n=98)	Group B (n=80)	χ^2 value	*P* value
Anorexia	7 (7.14)	6 (7.50)		
Sleep disorder	5 (5.10)	6 (7.50)		
Dry mouth	4 (4.08)	5 (6.25)		
Tremor	2 (2.04)	1 (1.25)		
Overall incidence	18 (18.37)	18 (22.50)	0.466	0.495

Table 5. WHOQOL-BREF results in the two groups after treatment ($\bar{x}$±sd)

Category	Group A (n=98)	Group B (n=80)	t	P
Mental health	14.23±2.26	11.33±2.84	7.587	<0.001
Physiological health	14.19±2.23	11.25±2.38	8.489	<0.001
Surrounding environment	12.92±2.01	11.68±2.41	3.743	<0.001
Social relations	13.82±2.07	11.72±2.91	5.614	<0.001

Quality of life in the two groups after treatment

After treatment, scores of mental health, physiological health, surrounding environment, and social relations via the WHOQOL-BREF scale in group A were significantly higher than those in group B (t=7.587, P<0.001; t=8.489, P<0.001; t=3.743, P<0.001; t=5.614, P<0.001). See **Table 5**.

Discussion

The pathogenesis of depression, a mood disorder disease, remains unknown. However, it is known to be closely related to psychological, social, and biological factors [17]. In clinical treatment of depression, the first objective is to relieve the clinical symptoms, improve treatment effects, and reduce self-harm and suicide rates. In the process of development of depression, patients often suffer from sleep disorders. Moreover, psychological intervention is often neglected in clinical treatment. This makes treatment compliance of patients lower, leading to drug and treatment efficacy failures [18, 19]. Persistent insomnia causes recurrence of depression and increases the risk of self-harm and suicide, bringing great pain to patients and families [20].

Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) and an antidepressant drug. It can block the reuptake of serotonin by the presynaptic membrane. Thus, it can improve the emotional state of patients and achieve good therapeutic effects on depressive mental disorders [21]. Fluoxetine has no affinity for histamine receptors and cholinergic receptors. Thus, it has no anticholinergic side effects, no analgesic effects, no hypertension induction, and less influence on the heart. It is effective in depressive mental disorders [22]. Gibbons et al. showed that fluoxetine can reduce clinical symptoms of depression patients in adults and the elderly. It can also reduce suicidal thoughts and behaviors [23]. In addition, a study by Gupta et al. confirmed that fluoxetine can effectively reduce HAMD scores of patients with severe depression. This may be realized by increasing serum levels of brain-derived neurotrophic factors and inhibiting levels of tumor necrosis factor-α [24]. Thus, fluoxetine has obvious benefits for patients with depression. Depression is often accompanied by stress, anxiety, negativity, pessimism, and other adverse psychological effects, leading to mental disorders in patients. These are the main factors causing insomnia. Emotional disorders affect the treatment of depression. The use of drugs, alone, without psychological intervention and emotional regulation, may not obtain good therapeutic effects [25]. In this study, fluoxetine and psychological intervention were applied to depression patients with insomnia. Results showed that HAMD scores and PSQI scores in groups A and B decreased significantly after treatment. Scores in group A decreased significantly, compared with group B, after treatment. Reduction rates in group A were significantly higher than those in group B. These indicate that fluoxetine combined with psychological intervention provides better effects for depression patients with insomnia than fluoxetine alone. This method can improve depression moods and sleep quality of patients. During the follow-up visits, WHOQOL-BREF scale scores were used to evaluate the quality of life of patients. Results showed that scores of mental health, physiological health, surrounding environment, and social relations via the WHOQOL-BREF scale in group A were significantly higher than those in group B after treat-

ment, indicating that fluoxetine combined with psychological intervention can improve the quality of life of patients with depression and insomnia. A study by Onkers et al. pointed out that psychological intervention can reduce depressive moods of the depressive elderly with diabetes or chronic obstructive pulmonary disease. It can also improve the quality of life of patients, in accord with current results [26]. Thus, psychological intervention can relieve bad moods and regulate depressive moods, improving the clinical efficacy of depressive patients with insomnia.

Although this study confirmed that fluoxetine combined with psychological intervention has better clinical effects on depressive patients with insomnia, there were still deficiencies. Quality of life levels of depressive patients with insomnia were not evaluated before treatment. Additionally, the causes of onset were not analyzed. Therefore, there are certain design defects which should be further supplemented in future research, further confirming the results of this study.

In summary, fluoxetine combined with psychological intervention provides good clinical effects for depressive patients with insomnia, compared to fluoxetine alone. This method can significantly reduce depression, improve sleep quality, and improve quality of life. Therefore, it is worthy of clinical application and promotion.

Disclosure of conflict of interest

None.

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